TPX2 promotes AURKA autophosphorylation

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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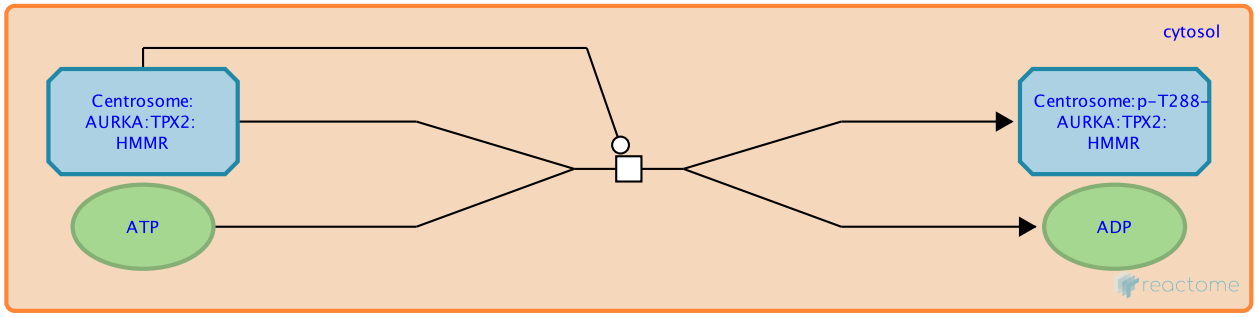
Stable identifier: R-HSA-8853419

Type: transition

Compartments: cytosol



TPX2 promotes aurora kinase A (AURKA) activation via autophosphorylation of AURKA on threonine residue T288. Continuous association of TPX2 with AURKA facilitates active state conformation of AURKA and may prevent inactivation of AURKA by protein phosphatases (Bayliss et al. 2003).

Molecular dynamic simulations suggest the existence of two TPX2-dependent switches for Aurora A activation. 1) TPX2 binding to Aurora A forces lysine residue K143 of AURKA into an “open” state, which pulls ADP out of the ATP binding site in AURKA to promote kinase activation. 2) Arginine residue R180 of AURKA undergoes a “closed” movement upon TPX2 binding, thus capturing phosphorylated threonine T288 of AURKA into a buried position and locking AURKA in its active conformation. The existence of two TPX2-dependent switches in AURKA activation was further verified by the analysis of two AURKA mutants (K143A and R180A) (Xu et al. 2011).AURKA activation is enabled through phosphorylation and TPX2 binding; these two activating switches act synergistically and withough a predefined order (Dodson and Bayliss 2012).

Literature references

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Editions

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